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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,614	09/05/2006	Masakazu Sato	Q96727	3121

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EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,614	SATO ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-14 are pending in this application.

Claim 12 is drawn to non-elected invention.

Response to Restriction

The election of group II, claims 1-6, in the Paper filed 4/30/09, is hereby acknowledged. There is no indication if the election is made with or without traverse. Therefore, it is deemed made without traverse. However, the restriction of claims 7-11 is now withdrawn. Claims 7-11 and new claims 13-14 are being examined with the elected invention in this Office action. Applicant also elects compound 194 for search purpose.

The restriction is still deemed proper and therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The compounds critical or essential to the practice of the invention, but not included in the claim(s) are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The scope of the claims is broader than the enabling disclosure of the specification. There are many known compounds which are ALK5 inhibitors within the scope of the claims but are not disclosed in the specification. By deleting the claims the rejection would be overcome.

Claims 7-11, are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for using the instant compounds as claimed. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, it is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965). "A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973). Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed utilities are not enabled for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988):

"The factors to be considered [in making an enablement rejection] have been summarized as a) the breadth of the claims, b) the nature of the invention, c) the state of the

prior art, d) the relative skill of those in that art, e) the predictability or unpredictability of the art, f) the amount of direction or guidance presented, g) the presence or absence of working examples, h) the quantity of experimentation necessary. a) The breadth of the claims encompasses many compounds with different substituents. b) The nature of the invention is using compounds as pharmaceuticals. The claims are drawn to treating various diseases arising from the inhibition of ALK5 not all of which are known today. Inhibition of ALK5 is not a practical utility under the US patent practice. One must read the specification into claims 7, 9-11 to ascertain their practical utilities contrary to several precedent decisions by the US courts and official practice. Even then, the claims would become duplicates of 8. Claims 7, 9-11 are attempts by applicant to claim treatment of diseases known and yet to be discovered arising from inhibition of ALK5. They are reach-through claims and are no longer patentable under the US patent practice. A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. *Ex parte Fressola*, 27 USPQ 2d 1608, BdPatApp & Inter. (1993). In patent examination, it is essential for claims to be precise, clear, correct, and unambiguous. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). Also, duplicates or substantial duplicate claims cannot be in the same application under the US patent practice.

In addition claims 10-11 are drawn to compounds beyond the enabling disclosure of the specification. In accordance with conclusive evidence in the prior arts and the specification not every compound capable of inhibiting ALK5 is applicant's invention or applicable for treating the diseases listed in claim 8. The diseases listed in claim 8 have different physiological mechanisms. The state of the prior art is that enzymes react in a lock and key mechanism and the structure of the compound must be specific. The presence of methyl instead of H changes the binding of a compound with an enzyme. For example, theophylline and caffeine differ by a

methyl group but one is used as a bronchodilator while the other is not used as a pharmaceutical. Hence, there is no absolute predictability or established correlation between different substituents on a core that they would behave in a certain way. The uncertainty presents one of ordinary skill in the art with obstacles and prevents her from accepting any therapeutic regimen on its face. d) The level of ordinary skill in the art of pharmaceutical art is high. e) The level of unpredictability in pharmaceutical art is very high, e.g. theophylline v. caffeine. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). f) The specification listed diseases for which the instant compounds are applicable in claim 8. However, such are deemed speculations because there is no conclusive evidence that the compounds would work as claimed: correct the various physiological mechanisms of the diseases. The only assays disclosed in the specification are inhibition of Smad2/3 phosphorylation and hair follicle proliferation. While IC_{50} values for Smad2/3 inhibition are disclosed for few examples of the compounds no results are disclosed for the proliferation test. Event then, there is no explanation how the IC_{50} values correlate with each disease. g) Given the limited guidance in the specification one of ordinary skill in the art would have to perform significant amount of experiments to make and use the invention as claimed.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. By limiting the

claims to a specific method of use having support in the specification the rejection would be overcome.

Applicant must note that the requirement of 35 USC 112, is not what is obvious to one of ordinary skill in the art but a "full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same", *Lookwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997). See the status above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The 2 rings representing "A" in claim 1 are duplicates. When the top structure is flipped 180^{o} one obtains the bottom structure, and vice versa. By deleting one of the rings the rejection would be overcome.

Claim 9 cites the inhibitor is "an external medicine." It is not clear what applicant is claiming. There is no definition of what constitutes external and/or internal medicine, and which compounds of claim 1 are in each category. The claim is confusing and therefore indefinite. Appropriate correction is required.

Claims 7-11 are duplicates of claim 1. The claims cite intended use. Under the US patent practice intended use is not a limitation in a compound or composition claim. *In re Hack*, 114USPQ 161 (CCPA, 1957); In *re Craig*, 90 USPQ 33 (CCPA, 1951); *In re Brenner*, 82 USPQ 49 (CCPA, 1949). By deleting the claims the rejection would be overcome.

The phraseology "R1 is a phenyl with a 5 to 7 . . . and benzo(1,3)dioxol," lines 3-6, claims 13-14, renders the claims indefinite. The bicyclic rings are not hetero atoms, are formed by condensation of 3 atoms with the phenyl not 5-7 atoms, and cannot be both hetero aromatic and non-aromatic. The claims are not clear and therefore indefinite. By replacing the phraseology with "R1 is selected from benzothiazolyl, benzoxazolyl or benzo(1,3)dioxol" the rejection would be overcome.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaster et al., WO 01/62756 A1, and Bender et al., WO 02/40468 A1, individually.

Each prior art discloses compounds and compositions thereof, which are inhibitors of ALK5. See the abstracts and specific species.

Objection

Claims 1-11 are objected to for containing non-elected invention. The claims must be amended within the scope of the elected invention of group II as follows: X1 is S, X2 is C, R1 is benzothiazolyl, benzoxazolyl or benzo(1,3)dioxol.

Specification

There is no brief description of the figure and other required subheadings in the specification. See the MPEP for the proper format.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1625

June 1, 2009